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Ambient temperature and risk of first primary basal cell carcinoma: A nationwide United States cohort study

D. Michal Freedman [a,*], Cari M. Kitahara [a], Martha S. Linet [a], Bruce H. Alexander [b], Gila Neta [a,1], Mark P. Little [a], Elizabeth K. Cahoon [a]

[a] Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, DHHS, Rockville, MD, USA
[b] Division of Environmental Health Sciences, School of Public Health, University of Minnesota, Minneapolis, MN, USA

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ABSTRACT

The Earth's surface is warming and animal studies have shown higher temperatures promote ultraviolet radiation (UVR) skin carcinogenesis. There are, however, no population studies of long-term temperature exposure and basal cell carcinoma (BCC) risk. We linked average lifetime summer ambient temperatures (based on weather station data) and satellite-based UVR estimates to self-reported lifetime residences in the U.S. Radiologic Technologists' cohort. We assessed the relationship between time-dependent average lifetime summer ambient temperature (20-year lag) in quintiles and BCC in whites, using Cox proportional hazards regression. Risks were adjusted for time-dependent lagged average lifetime UVR and time outdoors, body mass index, eye color, and sex (baseline hazard stratified on birth cohort). During a median 19.4 years follow-up, we identified 3556 BCC cases. There was no significant trend in risk between temperature and BCC. However, BCC risk was highest in the fourth quintile of temperature (Q4 vs. Q1; hazards ratio (HR) = 1.18; 95% confidence interval (CI) = 1.06–1.31, *p*-trend = 0.09). BCC risk was strongly related to average lifetime ambient UVR exposure (Q5 vs. Q1; HR = 1.54 (95% CI = 1.35–1.75, *p*-trend = <0.001)). Future studies of temperature and BCC risk should include a broad range of UVR and temperature values, along with improved indicators of exposure to temperatures and UVR.

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1. Introduction

Basal cell carcinoma (BCC) is the most common type of non-melanoma skin cancer (NMSC), and the most frequently diagnosed U.S. cancer [1]. The estimated U.S. incidence of NMSC is more than one million cases per year, of which about 70–80% are BCCs [2]. Although BCC is rarely fatal, it accounts for substantial disfigurement and health expenditures [1]. Epidemiologic studies of BCC have largely focused on the role of ultraviolet radiation (UVR), the main risk factor for BCC [2,3,1,4], but other factors are also involved [1].

Over several decades studies have suggested that temperature together with UVR might contribute to skin carcinogenesis [5–9]. Experimental animal studies demonstrated that elevated temperatures enhanced UVR carcinogenesis when UVR radiation was held constant [5,9]. Studies in human cell lines suggest that elevated temperatures may inhibit DNA repair in UV-irradiated cells [8] and may increase chromosomal aberrations in human keratinocytes [7]. One cross-sectional epidemiologic study found that NMSC incidence in 10 regions correlated with both ambient UVR and average daily maximum temperature in summer, despite a poor correlation between UVR and temperature in those areas [6].

Measurements show that the Earth's average surface temperature has risen 1.4° Fahrenheit (F) over the past 100 years, and additional warming of 2.0–11.5 °F over the 21st century is expected [10]. In 2010, The Interagency Working Group on Climate Change and Health, a U.S. governmental entity, outlined research needs in a report on the human health effects of climate change [11]. Among the cancer research needs identified was "elucidating the effects of ambient temperature on UVR-induced skin cancers, including the amplification of non-melanoma skin cancers."

The purpose of this study is to explore the association between long-term ambient temperature and subsequent BCC risk, while accounting for historic ambient UVR exposure, time outdoors, and other relevant factors. This study, which relies on data from the U.S. Radiologic Technologists (USRT) Study, a large nationwide cohort that draws members from all 50 states, is the first, to our knowledge, to assess BCC risk in a wide geographic population

* Corresponding author at: 9609 Medical Center Drive, 7E358, Rockville, MD 20850, USA. Tel.: +1 240 276 7394.
E-mail address: freedmam@mail.nih.gov (D. Michal Freedman).
[1] Current address: Division of Cancer Control and Population Sciences, National Cancer Institute, NIH, DHHS, Rockville, MD, USA.

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with estimates of historic ambient temperature and solar UVR exposures, and other key factors.

2. Materials and methods

2.1. Study population

The USRT Study comprises a cohort of U.S. radiologic technologists who were certified by the American Registry of Radiological Technologists for at least two years between 1926 and 1982 [12]. Detailed information on the study has been previously provided [12]. Three questionnaires were self-administered to the study members. A first questionnaire (1983–1989) provided information on height, weight, smoking behavior, as well as work history, cancer history, and other factors. A second questionnaire (1995–1998) also ascertained incident cancers and updated earlier information. The third survey (2003–2005) included information on eye and hair color, complexion, residential history and summer time outdoors, as well as cancer diagnoses. The USRT Study has been approved annually by the human subject review boards at the University of Minnesota and the National Cancer Institute and subjects gave their written, informed consent.

We restricted the study population to white participants who answered the first and/or second questionnaires, as well as the third questionnaire, and were cancer-free as of the baseline questionnaire (the earlier of the first or second questionnaire), $N = 66{,}362$. We then excluded participants who had omitted information on their residential locations ($N = 1792$) or for whom ambient UVR could not be calculated ($N = 4$), resulting in a study population of $N = 64{,}566$.

Eligible cases included only first primary BCC cases that were ascertained from the second or third questionnaires. BCC was defined as ICD-10 = C44 and morphology = 809–811×. Among the 3330 respondents reporting BCC, pathology reports and medical records were obtained for 1598 (48%). Of these, records validated the BCC diagnosis for 1527 (96%). We excluded 71 cases that were incorrectly reported as BCC and added 297 subjects with BCC found after validating other cancers. Based on the high validation rate, we included BCCs for which medical records were unavailable ($n = 1732$), bringing the total to 3556 BCC cases.

2.2. Data collection

The baseline questionnaires provided sex, body mass index (BMI), smoking history, and education at baseline. Occupational ionizing radiation skin dose to the head and neck, the most common sites for BCC [1], was estimated based on badge records and other factors [13]. The third survey provided data on eye and hair color, complexion, and residential history, as well as summer time outdoors.

UVR exposures derived from linking residential locations for up to five age groups (<13; 13–19; 20–39; 40–64; ⩾65 years) with the Total Ozone Mapping Spectrometer (TOMS) database (http://toms.gsfc.nasa.gov) maintained by the National Aeronautics and Space Administration (NASA). Residential locations (based on a 1.25° by 1° (longitude × latitude) grid) were linked to daily ambient UVR based on an estimated erythemal exposure level, which is an index of biological damage of Caucasian skin to sunburn (erythema). Values were averaged over the period collected by one satellite, Nimbus-7, (1978–1993), for June 1 through August 31 each summer, to provide stable estimates for each location ($n = 903$) and because satellite measurements were limited to some exposure periods. Temperatures were derived from meteorological data collected by U.S. weather stations and maintained by the National Climatic Data Center (NCDC) of the National Oceanic and Atmospheric Administration. Summer average daily mean temperatures (June 1–August 31) were averaged over 1971–2000 for each weather station, with a total of 7937 U.S. weather stations (NCDC Data set 9641C), again to provide stable estimates and because temperature data was limited to some exposure years. For each participant, average lifetime summer ambient temperatures and UVR levels were assigned based on combinations of residence and age at residence (over the five age groups set forth above), using data from the nearest weather station and TOMs grid cell, respectively, using ArcGIS 9.1 software (ESRI 2005).

2.3. Statistical analysis

Hazard ratios (HRs) and 95% confidence intervals (CIs) were computed using Cox proportional hazards regression, with age as the time-scale, which adjusts for age in all models to permit a time-dependent analyses of covariates [14]. Subjects were followed from baseline until the earliest of the third questionnaire or the diagnosis of the first cancer. In our primary analysis, we used time-dependent average lifetime ambient summer temperature, average lifetime ambient summer UVR and average lifetime summer time outdoors, all with a 20-year lag period because studies suggest that the latency for BCC may be 20 or more years [15–20]. Thus, for example, if a subject entered the study at age 40, that person's average cumulative exposure at entry was calculated at age 20 and changed as they aged if they subsequently moved. HRs with unlagged exposures were also calculated. In all analyses, cut-points for time-dependent variables were based on quintile cut-points defined at the end of follow-up (or the end of follow-up lagged by 20 years, if a lagged analysis), so that cut-points were fixed over time, but individual exposures could move between time-dependent categories.

We examined characteristics presented in Table 1 as potential confounders. In the principal analysis, in addition to lagged average lifetime summer ambient temperature, all models *a priori* included age (as the time-scale), sex, average lifetime summer ambient UVR (continuous, similarly lagged), average lifetime summer time outdoors (quintiles, also lagged), with the baseline hazard stratified on birth cohort (5-year groups). BMI (<25, 25–<30, ⩾30; unknown, kg/m^2) at baseline was chosen *a priori* because BMI is strongly negatively related to BCC risk in this cohort [21]. The only additional factor to be included in the final model was eye color (blue; green/blue; grey/green; hazel; light brown; dark brown; other; unknown) because it changed the HRs by more than 10%. The other variables did not change the HRs by more than 10% and were not included (i.e., every smoker (yes; no; unknown); complexion (light; medium; dark; other; unknown); hair color (blonde; red; brown; black; other; unknown); education (grade school; high school; rad tech program; college; graduate school; other; unknown); occupational ionizing radiation dose (continuous). Tests for trend treated quintiles as a continuous ordinal variable. The same covariates above were included in all the analyses (i.e., age, sex, ambient UVR, ambient temperature, time outdoors, BMI, eye color, and birth cohort in the baseline hazard).

Missing values for variables were coded as a separate "missing" category except for average lifetime summer ambient temperature, average lifetime summer ambient UVR, and average lifetime time outdoors. For these, values were imputed based first on the values for the nearest subsequent age interval with available values and then, on the nearest earlier age interval, if subsequent data were unavailable. A separate missing category was created for time outdoors only when no values were available for any age interval (<5% of participants).

In addition, we assessed the HRs for average lifetime summer ambient temperature by quintile of average lifetime summer ambient UVR exposure to examine whether temperature was

Table 1
Demographic and personal characteristics by quintiles of ambient average lifetime summer temperature (lagged by 20 years) in the U.S. Radiologic Technologists study, $N = 64{,}566$.

Characteristics	Ambient average lifetime summer temperature[a]				
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Sex, female (%)	80.5	82.9	79.2	78.2	76.7
Age, median (years)[b]	37.3	36.6	36.7	37.1	37.7
College or graduate education (%)[c]	38.2	37.2	40.0	40.9	40.2
Body mass index, median (kg/m^2)[b]	22.9	22.8	22.9	23.0	23.0
Ever smokers (%)[b]	49.4	50.4	50.0	51.4	49.9
Complexion, self-reported light skin (%)[c]	37.8	37.9	37.3	35.8	33.0
Hair color, red or blond (%)[c]	18.5	18.7	17.9	18.7	18.3
Eye color, blue (%)[c]	27.6	26.4	26.2	24.4	21.7
Ambient summer UVR exposure, median, (J/m^2)[d]	172.8	178.3	185.4	196.3	223.6
Time outdoors (summer) hrs/week, median[d]	19.0	18.9	18.6	18.7	18.0
Occupational ionizing radiation dose, median (cGy)[b]	4.1	4.0	3.9	4.2	4.8
Follow-up time, median (years)[d]	19.4	19.4	19.4	19.3	18.9

[a] Average lifetime summer (June–August) temperature (lagged by 20 years) as of the exit date; quintiles: 1st, 46.3–69.0; 2nd, 69.0–71.2; 3rd, 71.2–73.3; 4th, 73.3–76.6; 5th, 76.6–93.6 F°. Missing included in the denominator.
[b] As of baseline.
[c] As of third questionnaire (2003–2005).
[d] As of exit date.

associated with BCC risk within narrow UVR strata. To ensure adequate case numbers by temperature category, we combined temperature quintile categories (up to three) where a single category included fewer than 50 cases.

In addition to assessing risks associated with summer average daily mean temperature exposure, we also assessed summer average daily maximum temperature exposure, controlling for the same covariates as in the summer average daily mean temperature. Finally, we undertook a sensitivity analysis restricted to those BCCs that were validated with medical records.

We also assessed the correlation between average lifetime summer ambient temperature and average lifetime summer ambient UVR by quintiles. Tests were two-sided and p values were considered significant at the 0.05 level. Analyses were conducted with SAS (Version 9.2, SAS Institute, Inc., and Cary, NC).

3. Results

During a median follow-up of 19.4 years in a study population of 64,566 white respondents who were cancer-free at study entry, we identified 3556 BCC cases in 790 men and 2766 women. Compared to those with the lowest lagged average lifetime summer ambient temperatures (1st quintile), participants with the highest average lifetime summer ambient temperatures (5th quintile) were less likely to report having blue eyes and fair skin, more likely to have lived in high average lifetime summer ambient UVR areas and to have spent less time outdoors (Table 1).

BCC risk generally increased modestly across quintiles 1–4 of lagged average lifetime summer ambient temperatures, reaching the highest risk in the fourth quintile (HR = 1.18; 95% CI = 1.06–1.31) before declining in the 5th quintile, p-trend = 0.09 (Table 2). The sensitivity analysis restricted to validated cases did not change the HRs for each quintile of summer temperature or p-trend (data not shown). In the unlagged analysis, the HRs were similar but somewhat lower (Q4 vs. Q1; 1.14 (95% CI = 1.02–1.27), $p = 0.10$) (Suppl. Table 1). When we examined HRs associated with quintiles of summer average daily maximum temperatures, we found no associations, with the highest HR in the fourth quintile at HR = 1.05 (95% CI = 0.94–1.17) and a p-trend = 0.49 (data not shown).

BCC risk was strongly related to lifetime average summer ambient UVR exposure (Q5 vs. Q1, HR = 1.54 (95% CI = 1.35–1.75), p-trend = <0.001), Table 2. In contrast, there was no statistically significant trend between self-reported average lifetime summer time outdoors and BCC risk.

Table 2
Hazard ratios (HR) and 95% confidence intervals (CI) of first primary basal cell carcinoma by quintile of average lifetime summer ambient temperature, ultraviolet radiation, and time outdoors lagged by 20 years, in the U.S. Radiologic Technologists study.

	Range	Median	No. cases	HR	95% CI	p-Trend
Temperature[a,b]						
Q1	46.3–69.0	67.5	646	1.00		
Q2	69.0–71.2	70.2	664	1.08	0.97–1.20	
Q3	71.2–73.3	72.2	689	1.07	0.96–1.19	
Q4	73.3–76.6	74.7	771	1.18	1.06–1.31	
Q5	76.6–93.6	79.4	786	1.07	0.95–1.20	0.09
Ultraviolet radiation[c]						
Q1	75.8–175.6	170.0	600	1.00		
Q2	175.6–183.7	179.2	654	1.06	0.94–1.20	
Q3	183.7–196.2	187.7	663	1.01	0.88–1.15	
Q4	196.2–220.5	206.7	744	1.24	1.09–1.42	
Q5	220.5–312.2	236.7	895	1.54	1.35–1.75	<0.0001
Time outdoors[d]						
Q1	0–10.8	7.8	641	1.00		
Q2	10.8–16.3	13.9	677	1.18	1.06–1.31	
Q3	16.3–21.2	18.6	670	1.22	1.09–1.36	
Q4	21.2–26.9	24.0	659	1.11	0.99–1.23	
Q5	26.9–38.5	30.9	793	1.12	1.00–1.24	0.18

[a] HR adjusted for sex, BMI (<25; 25–<30; ⩾30 kg/m^2; missing), eye color (categories), average lifetime summer time outdoors (quintiles), average lifetime summer UVR (continuous), with the baseline hazard stratified on birth cohort (5-year categories). P-trend values based on categories treated as continuous ordinal values (quintiles).
[b] Fahrenheit scale.
[c] Erythemal exposure, (J/m^2); HRs adjusted for covariates as in temperature model but including temperature (quintiles). P-trend values based on categories treated as continuous ordinal values (quintiles).
[4] Hours/week; case count does not sum to 3556 because some participants did not report time outdoors (missing, $n = 116$ cases; 2691 non-cases). HRs adjusted for covariates as in temperature model but including temperature (quintiles). P-trend values based on categories treated as continuous ordinal values (quintiles).

In additional analyses examining temperature and BCC risk stratified by quintile of average lifetime summer ambient UVR exposure, the lowest risk was observed in the lowest temperature category across all UVR strata (Table 3). Within the three lowest UVR strata, the highest risks were associated with the highest temperature categories, and the trend was statistically significant in the third UVR strata. In the fourth UVR strata, risk was similarly

Table 3
Hazard ratios (HR) and 95% confidence intervals (CI) of first primary basal cell carcinoma by average lifetime summer ambient temperature stratified by level of average lifetime summer ambient ultraviolet radiation (UVR), lagged by 20 years, in the U.S. Radiologic Technologists study.[a]

UVR quintile[b]	Temperature range (°F)	No. cases	HR	95% CI	*P*-trend
Q1	46.3–69.0	372	Ref		
	69.0–71.2	189	1.12	0.93–1.35	
	71.2–93.6	39	1.22	0.87–1.70	0.13
Q2	46.3–69.0	84	Ref		
	69.0–71.2	274	1.16	0.90–1.48	
	71.2–73.3	243	1.09	0.84–1.40	
	73.3–93.6	53	1.19	0.84–1.69	0.60
Q3	46.3–71.2	118	Ref		
	71.2–73.3	224	1.01	0.80–1.26	
	73.3–93.6	321	1.21	0.98–1.50	0.03
Q4	46.3–71.2	96	Ref		
	71.2–73.3	73	1.18	0.87–1.60	
	73.3–76.6	286	1.18	0.93–1.60	
	76.6–93.6	289	1.16	0.93–1.50	0.28
Q5	46.3–69.0	102	Ref		
	69.0–71.2	75	1.26	0.93–1.69	
	71.2–73.3	114	1.50	1.15–1.97	
	73.3–76.6	136	1.24	0.96–1.61	
	76.6–93.6	468	1.13	0.91–1.41	0.94

[a] HR adjusted for sex, BMI (<25; 25–<30; ⩾30 kg/m^2; missing), eye color (categories), average lifetime summer time outdoors (quintiles) and average lifetime UVR (continuous) with the baseline hazard stratified on birth cohort (5-year categories). *P*-trend based on continuous ordinal values.

[b] The analysis was based on quintiles of temperature. When there were <50 BCC cases in a quintile, quintiles were combined. Quintiles of temperature, which had uniform cut-points, were combined as follows: in UVR quintile 1, we combined temperature Q3–Q5; in UVR quintile 2, we combined temperature Q4–Q5; in UVR quintile 3, we combined Q1–Q2 and Q4–Q5; in UVR quintile 4, we combined temperature Q1–Q2; and in UVR quintile 5, all temperature quintiles were presented.

elevated across all temperature categories above the reference category. In the highest UVR strata risk rose until the median temperature category and then declined.

The correlation between average lifetime summer ambient UVR and temperature in quintiles was 0.65. The distribution of cohort members by combined UVR/temperature quintiles is presented in Table 4.

Table 4
Distribution of participants by quintiles of ambient temperature and quintiles of UVR, lagged by 20 years in the U.S. Radiologic Technologists study.[a]

UVR	Ambient temperature, N (%)					Total
	Q1	Q2	Q3	Q4	Q5	
Q1	8013 (*62.1*)	1625 (*12.7*)	718 (*5.5*)	989 (*7.7*)	1568 (*12.1*)	12913 (*20.0*)
Q2	4149 (*32.1*)	5156 (*40.2*)	1637 (*12.6*)	939 (*7.3*)	1032 (*8.0*)	12913 (*20.0*)
Q3	698 (*5.4*)	4998 (*39.0*)	4678 (*36.0*)	1151 (*8.9*)	1299 (*10.1*)	12824 (*19.9*)
Q4	26 (*0.2*)	1031 (*8.0*)	5418 (*41.7*)	4758 (*36.9*)	1768 (*13.7*)	13001 (*20.1*)
Q5	25 (*0.2*)	10 (*0.2*)	548 (*4.2*)	5074 (*39.3*)	7249 (*56.1*)	12915 (*20.0*)
Total	12911 (*20.0*)	12829 (*19.9*)	12999 (*20.1*)	12911 (*20.0*)	12916 (*20.0*)	64566 (*100.0*)

[a] Temperature quintiles (Q1–Q5): 46.3–69.0; 69.0–71.2; 71.2–73.3; 73.3–76.6; 76.6–93.6 °F UVR quintiles (Q1–Q5): 75.8–175.6; 175.6–183.7; 183.7–196.2; 196.2–220.5; 220.5–312.2 J/m^2.

4. Discussion/conclusion

In this nationwide cohort study, we did not find a statistically significant trend in the relationship between average lifetime summer ambient temperature and BCC risk, after accounting for average lifetime summer ambient UVR exposure, average lifetime summer time outdoors, birth cohort, age, sex, BMI, and eye color. However, risk was lowest in the first quintile of temperature exposure and highest in the fourth quintile, with a suggestive trend in the risk relationship. Moreover, when we examined the BCC association with elevated average summer temperature in each stratum of ambient UVR exposure, we found that risks were also lowest in the lowest temperature categories and highest in the highest or penultimate temperature category in all but the fifth UVR strata. The relationship between average lifetime summer ambient UVR and BCC risk, in contrast, was substantially stronger with a highly significant trend, as would be expected [6].

Previous research supports the hypothesis that higher temperatures contribute to skin cancer. In animal experimental studies, investigators can control independently for UVR and ambient temperature [5,9,22]. An early animal study demonstrated that mice housed at high temperatures (approximately 95–100 °F) who received UVR from a mercury vapor lamp for 30 min/day 6 days/week developed tumors at an accelerated rate compared to mice housed at room temperature (73 °F) with the same UVR exposures [22]. A subsequent study subjecting mice to combinations of temperatures (90 °F vs. 75 °F) and short interval UVR daily vs. no UVR also found that mice kept in a hot environment developed skin tumors at a faster rate and in higher numbers than mice exposed to UVR at room temperatures.

The applicability of such experimental animal studies to human beings depends on whether the experimental conditions are relevant to real-life human conditions, whether carcinogenic processes [6] are comparable, and differences in thermal mechanisms between mice and human beings [5,9,22]. For example, the experimental animal conditions involved round-the-clock elevated temperatures, which are inapplicable to those human beings who can escape the heat for much of the day. It is not known whether short interval elevated temperatures accelerate carcinogenesis. Also, with regard to thermoregulation, mice are less able than humans to regulate skin temperature [5], which, to the extent skin temperature contributes to accelerated carcinogenesis in animals, may affect the applicability of experimental studies to humans. While there are few studies of human cell lines examining potential mechanisms of thermal carcinogenesis, some studies have shown that elevated temperatures can induce DNA strand breaks, possibly resulting in chromosomal gains and losses [7] and induce lower rates of DNA repair [8]. It has also been hypothesized that high temperatures may elevate skin cancer risk by a heat stress response that inhibits cell death-signaling pathways, allowing DNA-damaged cells to proliferate.[23].

One previous epidemiologic study by van der Leun et al. [6] examined maximum daily summer temperatures (averaged over 30 years) and BCC incidence in whites in one year in 10 U.S. regions, controlling for UVR measured during a single year (across all seasons) using Robertson-Berger meters (state-wide measures). Thus, while the study found BCC incidence positively related to temperature increase, van der Leun et al. acknowledge that the study was exploratory with limited data. The van der Leun et al. study differed from ours in several key respects. It was an ecologic study, which used incidence data for the 10 locations, without individual information on lifetime residential history (and thus without temperature/UVR exposure data associated with individuals' residences over their lifetime), and without summer time outdoors or any personal sun sensitivity or other covariate information.

Further, we examined average mean and average maximum summer daily temperatures, whereas van der Leun examined only average maximum temperatures. In addition, whereas we had access to UVR data averaged over a long timespan (16 years) and specific to relatively small geographic areas (1.25° by 1° (longitude × latitude) grid) across the entire U.S., the prior study used a single year of state-wide UVR data for 10 locations. Thus, our study made several improvements over the prior cross-sectional/ecologic study.

In the present study, as noted, however, we did not find a trend in the relationship between average summer temperature and BCC risk. Estimating exposure to temperature is especially challenging. Our failure to find a risk trend related to temperature may reflect our limited ability to estimate the duration of participants' exposure to outdoor temperatures, given the difficulties of recalling time outdoors over long periods. There were other limitations to our estimates of exposure to temperature. Our source of data was limited to average time outdoors in *summer* months, not throughout the year, despite substantial differences in temperatures in other seasons by region. Moreover, we did not have potentially relevant hourly exposure information, such as outdoor time of day preferences or opportunities (e.g., noontime vs. early evening). During their careers as indoor workers, many participants would have had limited exposures to peak temperatures during the day, which potentially contributed to the lack of associations with average maximum summer temperatures. We also lacked information on behavioral preferences for shade vs. sun, access to air conditioning inside the home over the lifespan, and personal behaviors such as use of saunas and electric blankets, which would affect skin exposure to elevated temperatures regardless of outdoor temperatures.

It is also possible that the positive associations we observed with temperature reflect limitations of the data rather than a biologic relationship. Given the moderately high correlation ($r = 0.65$) between summer temperature and UVR, we cannot exclude the possibility that our measures of temperature partly captured residual measures of UVR, rather than an independent role for temperature.

Although the USRT cohort compiled data on lifetime residences, the recorded exposures are inevitably subject to misclassification. The task of identifying a single *usual* residence over long periods may involve misclassification when there are multiple residences. In addition, we did not have temperature and UVR data that corresponded precisely to specific calendar years, because some exposure periods preceded available ambient data. Instead, we used temperature and UVR for specific residences averaged across years, so that each year in a location corresponded to average temperatures and UVR over time in that place. Thus, temperature and UVR variability reflected geographic differences, which exceed local year-to-year UVR/temperature variations. Also, measures of ambient temperatures and UVR correspond to geographic areas (i.e., 7937 different weather stations across the U.S.), not the specific residences of participants, nor the various non-residential places to which they travel.

A strength of this study is that the USRT Study enlists participants from across the U.S., which ensures a wide range of UVR and temperature exposures. Access to TOMS (UVR) and temperature data through linkage to government databases provides estimates of lifetime exposures for specific locations. The validity of the ambient UVR metric is supported by the expected relationships observed between average lifetime summer ambient UVR exposure and BCC. The USRT Study also allowed us to account for important demographic and behavioral factors for participants in our models.

In conclusion, we did not find a dose–response relationship between ambient temperature and BCC risk. Rather BCC risk rose slightly as ambient temperature increased except for those living in the fifth temperature quintile, the hottest areas. Possibly our failure to find a dose–response relationship reflects various limitations in our exposure estimates. If feasible, it would be useful to explore temperature and skin cancer in other population-based studies that have a wide range of UVR/temperatures over participants' lifetimes and improved estimates of outdoor and indoor temperature exposures.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jphotobiol.2015.04.025.

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